Reaction Stereochemistry

A regioselective reaction: preferential formation of one constitutional isomer

$$A \longrightarrow B + C$$

more B is formed than C where B and C are constitutional isomers

A stereoselective reaction: preferential formation of a stereoisomer

$$A \longrightarrow B + C$$

more B is formed than C where B and C are stereoisomers

Stereoselectivity
vs.
Sterospecificity

Chiral Acids-Bases
Diastereomers

http://ep.llnl.gov/msds/orgchem/Chem226/stereo1.html

A stereospecific reaction: each stereoisomeric reactant produces a different stereoisomeric product or a different set of products

$$A \longrightarrow B$$

$$C \longrightarrow D$$

A and C are stereoisomers
B and D are stereoisomers

All stereospecific reactions are stereoselective
Not all stereoselective reactions are stereospecific

Many reactions convert achiral reactants to chiral products.

If all of the components of the starting state (reactants, catalysts, solvents, etc.) are achiral, any chiral products that will be formed are racemic mixtures.

"Optically inactive starting materials can't give optically active products."

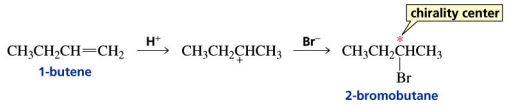
In order for a substance to be optically active, it must be chiral and one enantiomer must be present in greater amounts than the other.

Table 5.2 Stereochemistry of Alkene Addition Reactions

Reaction	Type of addition	Stereoisomers formed
Addition reactions that create one asymmetric carbon in the product		1. If the reactant does not have an asymmetric carbon, a pair of enantiomers will be obtained (equal amounts of the *R* and *S* isomers). 2. If the reactant has an asymmetric carbon, unequal amounts of a pair of diastereomers will be obtained.
Addition reactions that create two asymmetric carbons in the product		
Addition of reagents that form a carbocation or radical intermediate	syn and anti	Four stereoisomers can be obtained[a] (the cis and trans isomers form the same products)
Addition of H_2	syn	cis ⟶ erythro enantiomers[a]
Addition of borane		trans ⟶ threo enantiomers
Addition of Br_2	anti	cis ⟶ threo enantiomers trans ⟶ erythro enantiomers[a]

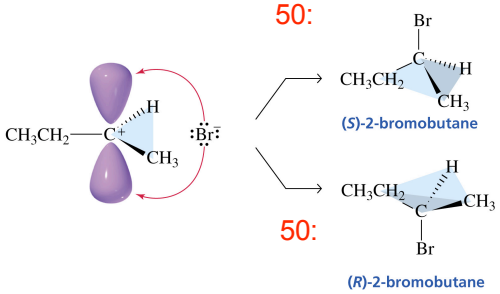
[a] If the two asymmetric carbons have the same substituents, a meso compound will be obtained instead of the pair of erythro enantiomers.

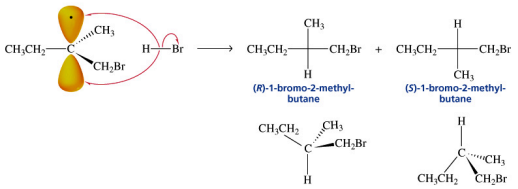
Stereochemistry of Electrophilic Addition Reactions of Alkenes



Can you determine the absolute configuration of the product?

Addition reactions that form one asymmetric carbon: How much of each isomer forms?



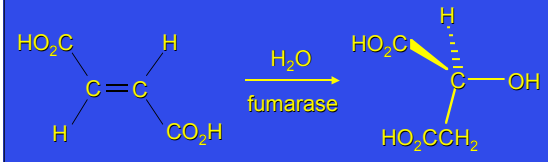


Many biochemical reactions convert an achiral reactant to a single enantiomer of a chiral product

Reactions in living systems are catalyzed by enzymes, which are enantiomerically homogeneous.

The enzyme (catalyst), which is chiral and optically active, is part of the reacting system, so such reactions don't violate the generalization that "Optically inactive starting materials can't give optically active products."

Example

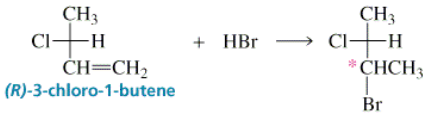


Fumaric acid
Achiral

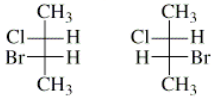
(*S*)-(–)-Malic acid
Single enantiomer

Lactic acid: Chem 226 Web pages
http://ep.llnl.gov/msds/orgchem/Chem226/stereo1.html

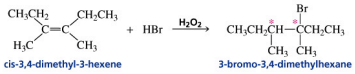
Addition reactions that form an additional asymmetric carbon



stereochemistry of the product

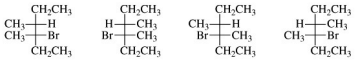


Addition reactions that form two asymmetric carbons
A radical reaction intermediate

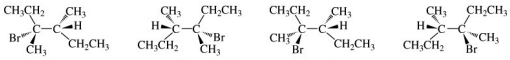


cis-3,4-dimethyl-3-hexene → 3-bromo-3,4-dimethylhexane

stereochemistry of the product

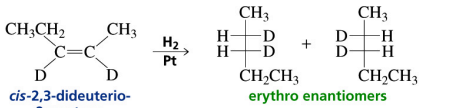


Fischer projections of the stereoisomers of the product



perspective formulas of the stereoisomers of the product

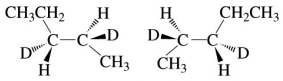
Stereochemistry of Hydrogen Addition (Syn Addition)



cis-2,3-dideuterio-2-pentene

erythro enantiomers

Fischer projections of the products

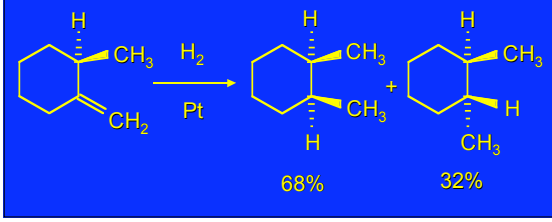


perspective formulas of the products

A stereoselective reaction

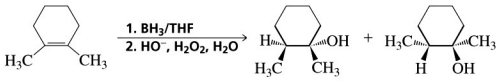
- What is the optical yield for the reaction? *36%= Pure - Racemic*
- Will the physical properties of the products be the same?

No, diastereomers have different physical properties.



Stereochemistry of Hydroboration–Oxidation

50: 50



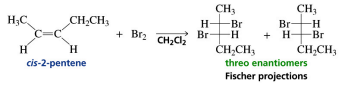
Syn addition, that is from the same side: either top or bottom.

What is the distribution and relationship of the products?

Enantiomers or Diastereomers?

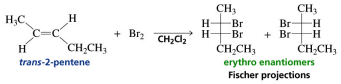
Enantiomers

Addition reactions that form a bromonium ion (anti addition)



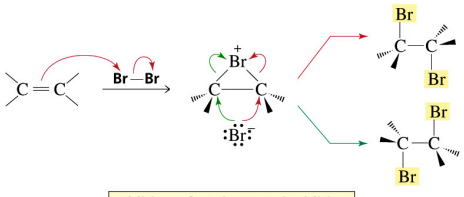
cis-2-pentene → threo enantiomers

Fischer projections



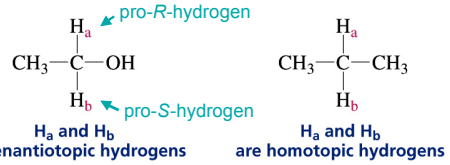
trans-2-pentene → erythro enantiomers

Fischer projections



addition of Br_2 is an anti addition

Stereochemistry Vocabulary

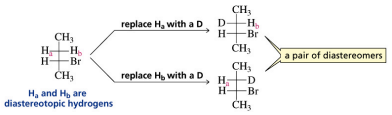


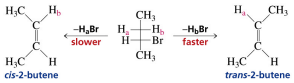
H_a and H_b are enantiotopic hydrogens

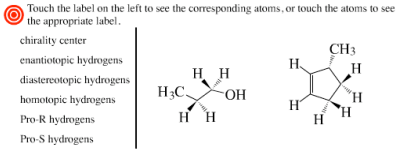
H_a and H_b are homotopic hydrogens

Enantiotopic hydrogens have the same chemical reactivity and cannot be distinguished by achiral agents, but they are NOT chemically equivalent toward chiral reagents (Most relevant in biochemistry/physiology.)

Diastereotopic hydrogens do not have the same reactivity with achiral reagents







Applying the Principle: Resolution of Enantiomers

Separation of a racemic mixture into its two enantiomeric forms.

Resolution of a Racemic Mixture

(*R*)-acid (*S*)-acid enantiomers

(*S*)-base →

(*R*,*S*)-salt (*S*,*S*)-salt diastereomers

(*R*,*S*)-salt (*S*,*S*)-salt

HCl HCl

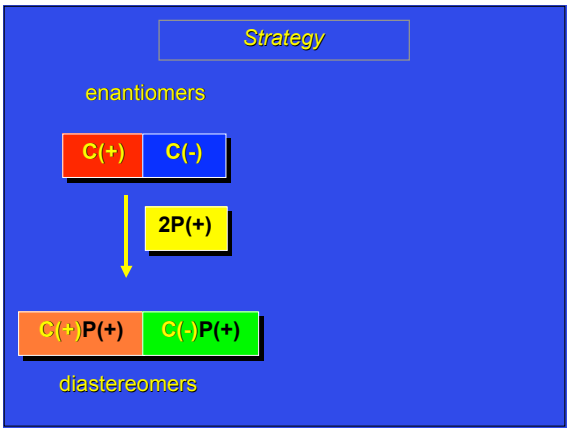
(*S*)-baseH⁺ + (*R*)-acid

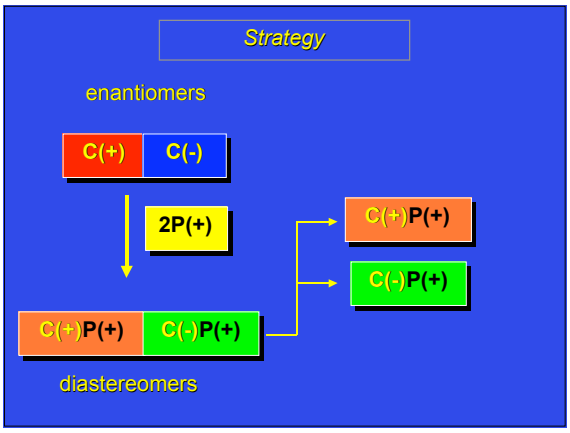
(*S*)-baseH⁺ + (*S*)-acid

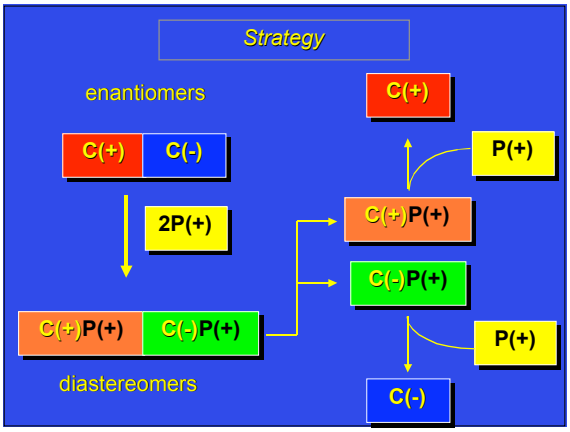
Strategy

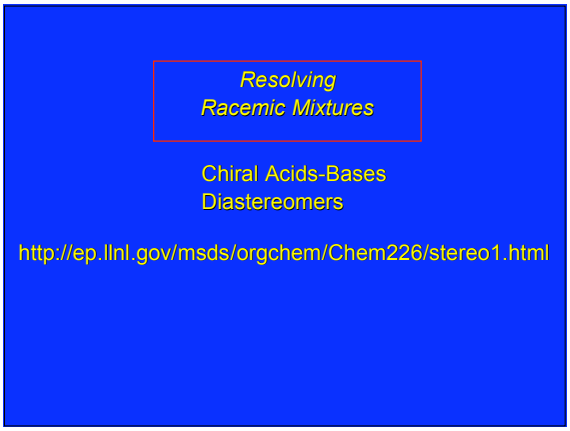
enantiomers

C(+) **C(-)**


Strategy
enantiomers
C(+)
C(-)
2P(+)
C(+)P(+)
C(-)P(+)
diastereomers


Strategy
enantiomers
C(+)
C(-)
2P(+)
C(+)P(+)
C(-)P(+)
C(+)P(+)
C(-)P(+)
diastereomers


Strategy
enantiomers
C(+)
C(-)
2P(+)
C(+)P(+)
C(-)P(+)
diastereomers
C(+)
P(+)
C(+)P(+)
C(-)P(+)
P(+)
C(-)


Resolving
Racemic Mixtures
Chiral Acids-Bases
Diastereomers
http://ep.llnl.gov/msds/orgchem/Chem226/stereo1.html